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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/809,158	03/15/2001	Carol O. Cowing	LANCELL.002CP1	5364

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 03/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/809,158	COWING, CAROL O.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 60-85 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 60-62 and 64-85 is/are rejected.

7)☒ Claim(s) 63 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 11/21/2005.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 10, 2005 has been entered.

2. Claims 1, 4-11, 13-19, 21-24, 27-31, 37, 42, 51-55, 58 and 59 have been canceled. Claims 60-85 are pending and under consideration.

3. Acknowledgment is made of applicants claim to an earlier effective filing date through 09/176,044, filed 10/20/98, now U.S. 6,210,672. Upon review of the '672 patent it is noted that no support is provided for the formula (1) of claim 64, which differs from the compounds described in '672 patent (column 8-9) by the addition of the "W" moiety which can be a saturated or unsaturated chain consisting of C1-C10 alkyl, C1-C10 substituted alkyl, C7-C10 phenylalkyl, C10 -C16 substituted phenylalkyl, phenyl, substituted phenyl, naphthyl, substituted naphthyl, C3-C7 cycloalkyl and C3-C7 substituted cycloalkyl group, and wherein each terminus of the chain is bonded to the carbon C(R3R3') and C(R4R4'). Formula (1) also differs from the compounds of the '672 patent by the presence of quaternary carbons carrying both a R3 and a R3' as well as a R4 and a R4'. The '672 patent describes a structure on the top of column 9, wherein a single R3 and R4 group is present and wherein R3 and R4 may be linked for form a ring structure. This is inadequate support for the instant formulas (1) and (3) which allow for the presence of two quaternary carbons carrying a R3 and a R3' as well as a R4 and a R4'. Further, the compounds of the '672 patent do not provide adequate support for "X" of the instant application because none of the compounds listed in column 9 or implied by the structure at the top of column 9 of the '672 patent have a heteroatom other than an oxygen at the position indicated by the formulas 1, 2 and 3. It is noted that applicant has introduced a number of citations not in the instant specification cited art which was not published at the time of filing of the '672 patent, said art including the use of imiquimod (page 15, lines 20-28) the instant specification which is subject matter not contemplated by the '672 patent One of skill in the art

would reasonable conclude upon reading of the instant application, that applicant was not in possession of the genus of compounds of formulas 1 through 3 at the time the '672 patent was filed. Because applicant was not in possession of the genus of compounds on which the instant method claims rely, applicant was not in possession of the instant invention as of the filing date of the '672 patent. Accordingly, the priority date for the instant invention will be the March 15, 2001 filing date.

4. Text of Title 35, U.S. Code, not found in this action can be found in a previous action.

5. Claim 71 is objected to for the typographical error of "bihenylmaleate" rather than biphenylmaleate.

Appropriate correction is required.

6. Claim 71 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear how claim 71 further modifies claim 64. Claim 71 includes the species of N, N-diethyl toluamide and benzoic acid, both of which have only one carbonyl group, neither of which conform to the structural requirements of the formulas of claim 64.

7. Claims 60-62, 64-70, 72-76, 78-85 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 60-62, 82 ad 83 are method claims reliant on a "topical treatment" which in the absence of antigen is sufficient to increase the number of dendritic cells migrating to a lymphoid organ. Claims 61 specifies that the "topical treatment" is a lipophilic molecule capable of traversing the stratum corneum. Claim 62 specifies that the lipophilic molecule of less than 500 Daltons. Claim 72 specifies that the lipophilic molecule comprises a terpene. Claim 73 specifies

that the lipophilic molecule has a oil/water partition coefficient of greater than 1. Claims 64-70 and 85 specify a collection of structural elements encompassed by the formulas 1, 2 and 3 of claims 64 and 85.

The specification teaches that various structures which can be represented as formula 2, having "X" as an oxygen atom, represent compounds able of traversing the stratum corneum and causing an increase migration of dendritic cells into a draining lymph node. Claims 60-62 and 70-74, and dependent claims thereof, are reliant on a genus of topical treatments molecules which can be any small organic molecule sufficient to increase the number of dendritic cells migrating to a draining lymph node. This genus is highly variant encompassing organic molecules which have no structural similarity to the specific phthalates, maleates, succinates and fumarates taught by the specification, nor the N,N diethyl toluamide, camphor or benzoic acid. The genus of terpenes required by claim 72 is highly variant encompassing the most abundant components of the essential oils of plants and flowers, and can be broken down into monoterpenes, sesquieterpenes and diterpenes, including bicyclic, tricyclic or polycyclic terpenes (Streitwieser and Heathcock, Introduction to Organic chemistry, (text), 1976, pp. 643-645). The specification discloses only one species of said genus as camphor. This disclosure fails to describe the genus of terpenes because said genus contains members which differ significantly in structure from camphor. Claims 64-70. and dependent claims thereof are reliant on a genus of molecules having some structural requirements as listed in the claims. This genus is also highly variant because it encompasses a plethora of organic structures variant at X, R3, R3', R4, R4', and in the case of formula 1, W. These structures allow for a multitude of variant compounds comprising sulfur, nitrogen or oxygen in independent combinations as "X", R3, R3', R4 and R4' groups comprising hydroxyl, halogen, alkyl groups from 1 to 16 carbons, which are substitutes or unsubstituted carbons, the nature of said substitutions is unlimited; three to ten carbons in a ring, three to ten carbons in a ring which are also substituted, the nature of the substitution being unlimited, two to ten carbons encompassing at least one double bond; two to ten carbons encompassing at least one double bond and substitutions which are unlimited; two to ten carbons encompassing at least one triple bond; two to ten carbon encompassing at least one triple bond with substitutions which are unlimited; seven to 16 carbons which constitute a phenyl alky group; seven to sixteen carbons which constitute a phenyl alkyl group which is substituted, the

nature of the substitution being unlimited; as well as substituted phenyl, substituted napthyl. The specific species described by the specification (claim 71 and camphor) fail to describe the broad genuses of compounds encompassed by claims 64-70 and independent claims thereof because the phthalates, maleate, and fumarates partially describe formula 2 when "X" is oxygen. The tartarate of claim 71 partially describe formula 3 wherein "X" is oxygen and R3 is hydroxyl and R3' is hydrogen and R4 is hydrogen and R4' is hydroxyl. The succinate of claim 71 partially describes formula 3 wherein "X" is oxygen and R3 ,R3' R4 and R4' are all hydrogen. Thus, the large part of the genus of molecules encompassed by claims 64-70 and dependent claims thereof are not adequately described by the specification. One of skill in the art would reasonably conclude that applicant was not in possession of the genus of compounds encompassed by claims 60-62, 64-70, 72-76, 78-85. Because the specification fails to adequately describe a product on which a method claim relies, it follows that the method claims are also not adequately described.

8. Claims 60-62, 82 and 83 are rejected under 35 U.S.C. 102(b) as being anticipated by Daynes et al WO 91/04030.

Claim 60 is drawn to a method for vaccinating a mammal against a target antigen comprising introducing into the mammal by disruption of the stratum corneum an effective dose of the target antigen or an epitope thereof and administering to the mammal a topical treatment which in the absence of antigen is sufficient to increase the number of dendritic cells migrating to a lymphoid organ. Claim 61 embodies the method of claim 60, wherein the topical treatment comprises a lipophilic molecule capable of traversing the stratum corneum. Claim 62 embodies the method of claim 61 wherein the lipophilic molecule is less than 500 Daltons. Claim 82 embodies the method of claim 60 wherein the topical treatment further increases the number of antigen-bearing dendritic cells in the lymphoid organ by a factor of about 2 to 100 times the number found in an untreated mammal. Claim 83 embodies the method of claim 82 wherein the factor is about 5 to about 100 times.

Daynes et al teach a method comprising vaccinating a mouse in the hind footpad with OVA in CFA and applying DHEA or 1,25(OH)2D3, which are classified as "steroid hormone" by the inventor, topically to the skin sites above the site of vaccination (page 27, line 34 to page 28, line 2). Daynes et al do not teach that DHEA or 1,25(OH)2D3 is sufficient to increase the

number of dendritic cells migrating to a lymphoid organ in the absence of antigen, or increase the number of antigen bearing dendritic cells in a lymphoid organ by a factor of 2 to 100 or 5 to 100. However, DHEA and 1,25(OH)2D3 are lipophilic molecules applied topically to the mouse skin which modulate the immune response of said mouse to an injected antigen. The Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

9. Claims 60 and 77 are rejected under 35 U.S.C. 102(b) as being anticipated by Kost et al WO 88/00001 as evidenced by Mitragori et al (WO 00/35351).

Claim 70 embodies the method of claim 60, wherein the topical treatment is ultrasound.

Kost et al disclose a method of administering an antigen transdermally comprising applying ultrasound energy to the skin (page 5, lines 20-24). Ultrasound application to the skin meets the specific embodiment of disrupting the stratum corneum as evidenced by Mitragori et al who state that the ultrasound energy often results in damage to the skin (page 4, lines 2-3). Further, the instant specification teaches that ultrasound produced cavitational effects, including micro-bubbles that expand and contract in the stratum corneum, which meets the specific embodiment of "disrupting" the stratum corneum however transient. Neither Kost et al nor Mitragori et al disclose that the application of ultrasound energy would cause an increase the number of dendritic cells migrating to a lymphoid organ. However, this is a property taught to be inherent in the application of ultrasound energy as provided by the instant specification and thus would be inherent in the prior art method of Kost et al.

10. Claims 60-62, 64-70, 72-76 and 78-85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baumann et al (Journal of Immunology, 2000, Vol. 165, pp. 158-167) in view of Price et al (Journal of Experimental Medicine, 1997, Vol. 186, pp. 1725-1735).

Baumann et al teach a method comprising the subcutaneous immunization of mice with cryptococcal antigens (page 159, under the heading of "Cryptococcal Ags, immunization, and infection". Baumann et al teach that increases in stimulatory Langerhans cells in the lymph nodes draining the site of Ag deposition are needed to induce a protective anti-cryptococcal response (page 166, first column, lines 31-39). Baumann et al do not teach a topical treatment which in the absence of antigen is sufficient to increase the number of dendritic cells migrating to a lymphoid organ.

Price et al teach that topical exposure to chemical allergens results in the migration of epidermal Langerhans cells from the skin and accumulation as immunostimulatory dendritic cells in the draining lymph nodes (abstract, lines 1-3). Price et al specifically teach oxazolone as a chemical allergen having said properties (page 1726, under the heading of "Chemicals and Exposure"). Oxazolone is a lipophilic molecule of less than 500 Daltons.

It would have been prima facie obvious at the time the invention was made to apply oxazolone topically to the injection site. One of skill in the art would have been motivated to do so by the teachings of Baumann et al on the necessity of accumulating stimulatory Langerhans cells in the draining lymph nodes at the site of antigen deposition and the teachings of Price et al on the ability of oxazolone and other chemical allergens to stimulate migration of epidermal Langerhans cells to a draining lymph node. One of skill in the art would be motivated to induce a protective response to an administered antigen in order to produce an efficacious response from the vaccination.

11. Claims 60 and 77 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 7, 16-18 and 20 of U.S. Patent No. 6,210,672. Claims 60-76 and 78-85 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15 of US 6,210,672. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '672 patent anticipate the instant claims.

12. Claim 63 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and

any intervening claims.

13. All other rejections and objections as set forth or maintained in the previous Office action are withdrawn in light of applicants amendments.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 11 am to 10 pm, except Wed, Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
1/9/2006

KAREN A. CANELLA PH.D
PRIMARY EXAMINER